

embodiments methods are provided which can further include the administration of a second fugetactic or anti-fugetactic agent.

Each of the limitations of the invention can encompass various embodiments of the invention. It is, therefore, anticipated that each of the limitations of the invention involving any one element or combinations of elements can be included in each aspect of the invention.

These and other aspects of the invention, as well as various advantages and utilities, will be more apparent with reference to the detailed description of the preferred embodiments.

Brief Description of the Drawings

Fig. 1 describes the amino acid sequences of HSP 90 (SEQ ID NOS 1-3), HSP 84 (SEQ ID NOS 4-5), HSP 86 (SEQ ID NO: 6), HSP 60 (SEQ ID NO: 7) and L-plastin (SEQ ID NO: 8).

Fig. 2 provides the results of a transmigration assay using 1 in 2, 1 in 10 and 1 in 100 dilutions of EL4 24-hour conditioned media (EL4CM24).

Fig. 3 provides the results of a transmigration assay using negative gradients of heat inactivated or proteinase K digested EL4 24-hour conditioned media (EL4CM24) (1 in 2, 1 in 10 and 1 in 100 dilutions).

Fig. 4 provides the results of a transmigration assay using negative gradients of EL4 24-hour conditioned media (EL4CM24) with pertussis toxin treated murine lymphocytes and radicicol and Geldanamycin treated EL4CM24 (1 in 2, 1 in 10 and 1 in 100 dilutions).

Fig. 5 provides the results of an *in vivo* study of the migration of immune cells using EL4 24-hour conditioned media (EL4CM24).

Fig. 6 provides the results of EL4 24-hour conditioned media (EL4CM24) (I0.5 and HSF) run on SDS PAGE.

Fig. 7 provides the results of the ion exchange chromatography of the EL4 24-hour conditioned media (EL4CM24).

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Fig. 8 provides the results of a transmigration assay using EL4 24-hour conditioned media (EL4CM24) heat shocked at 42°C and treated with Brefeldin A.

Fig. 9 provides the mass peaks from the mass spectrometry analysis of a fraction of EL4 24-hour conditioned media (EL4CM24) that contained a protein of about 84/86 kDa.

Fig. 10 provides the mass peaks from the mass spectrometry analysis of a fraction of EL4 24-hour conditioned media (EL4CM24) that contained a protein of about 94 kDa.

Fig. 11 provides the mass peaks from the mass spectrometry analysis of a fraction of EL4 24-hour conditioned media (EL4CM24) that contained a protein of about 65 kDa.

Fig. 12 provides the MS-Fit and MS-Tag search results of a component protein of about 84 and 86 kDa (SEQ ID NOS 9-45, 121, and 46-51, respectively in order of appearance).

Fig. 13 provides the MS-Fit search results of a component protein of about 94 kDa (SEQ ID NOS 52-72, respectively in order of appearance).

Fig. 14 provides the MS-Fit and MS-Tag search results of a component protein of about 65 kDa (SEQ ID NOS 74-106, 121, and 107-118, respectively in order of appearance).

Fig. 15 provides the sequence alignment of human HSP 90-□ (SEQ ID NO: 119) and mouse HSP protein 84 (SEQ ID NO: 4).

Fig. 16 provides the sequence alignment of HSP 84 (SEQ ID NO: 4) and HSP 86 (SEQ ID NO: 120), both from the mouse.

Detailed Description of the Invention

It has now been discovered, according to the invention, that tumor cells elaborate both chemokines and other chemokinetically active substances which evoke a fugetactic or chemorepellent response from immune cells, thereby allowing the neoplastic cells to evade recognition and destruction by the host immune system. Using *in vitro* and *in vivo* assays it has now been demonstrated that culture supernatant (i.e.,

conditioned media) from the EL4 cell line has the ability to repel lymphocytes (i.e., to induce fugetaxis). It has been further shown that migration of lymphocytes away from EL4 24-hour conditioned media (EL4CM24) was diminished by heat inactivation and proteinase digestion of the conditioned media as well as with the use of the specific inhibitors (pertussis toxin and radicicol). Fractionation and subsequent tests on the conditioned media fractions resulted in the identification of agents which induce fugetaxis. Some of these agents show homology to heat shock proteins (HSPs) as well as L-plastin.

The present disclosure therefore provides, in part, agents with migratory cell repellent activity (hereinafter "fugetactic agents" and "fugetactic activity" or